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10/535,270	02/09/2006	Rex W. Newkirk	101927/43	5756

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EXAMINER	
MI, QIUWEN	
ART UNIT	PAPER NUMBER
1655	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,270	NEWKIRK ET AL.	
	Examiner	Art Unit	
	Qiuwen Mi	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 18 May 2005 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 5/18/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims Pending

Claims 1-20 are pending. Claims 1-20 are examined on the merits.

Claim Rejections –35 USC § 112, 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (c) recites the limitation "the neutral components". There is insufficient antecedent basis for this limitation in the claim. It is not clear what "the neutral components" are being referred to.

Although claims 2-20 are not specifically recited for containing indefinite matter, because these claims are dependant directly or indirectly upon claim 1, claims 2-20 necessarily comprise all of the limitations of claim 1. Because claims 2-20 do not remedy the indefiniteness of claim 1, these claims are also properly rejected under this statute.

Claim Rejection 112, 1st

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for producing inositol from plant material using phytase enzyme, does not reasonably provide enablement for a process for producing inositol from plant material using a phytase enzyme which does not include acid phosphatase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

It is well known in the art that phytase alone is not sufficient to enable complete conversion of phytate to inositol and inorganic phosphate, and purified phytase (Nevalainen et al (US 5,834,286), while effective in mediating the hydrolysis of phytic acid, was less effective in catalyzing hydrolysis of other similar phosphate-containing substrates. In contrast, purified pH 2.5 acid phosphatase, while relatively effective in hydrolyzing simpler phosphate, was relatively ineffective in catalyzing hydrolysis of phytic acid. The results support the notion of a coorperative enzymatic mixture wherein the products of a purified phytase might serve as a substrate for a purified pH2.5 acid phosphatase so that free inositol and inorganic phosphate are the ultimate products of the reaction (col 20, lines 47-60). It can be concluded that the probable hydrolytic end products of purified phytase enzymes are inositol di-and/or monophosphates. In contrast, purified acid phosphatase catalyzed degradation of phytate at pH2.5, producing inositol as an end product. As mentioned above, the invention only provides the description of

specification for being enabling for a process for producing inositol from plant material using phytase enzyme, does not provide enablement for a process for producing inositol from plant material using a phytase enzyme which does not include acid phosphatase. It is the opinion of the Examiner that Applicant is not enabled for producing inositol from plant material using a phytase enzyme which does not include acid phosphatase as instantly claimed. Considering this evidence, the skilled artisan, lacking information with regard to any inositol producing procedure using a phytase which does not include specification, while being enabling for a process for producing inositol from plant material using phytase enzyme, does not reasonably provide enablement for a process for producing inositol from plant material using a phytase enzyme which does not include acid phosphatase, would necessarily need to perform tedious trial and error protocols without expectation of success in order to ascertain what compound would provide for the specific therapeutic uses as described in the specification.

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; *however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112*; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment

provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved." (Emphasis added)

Due to the large quantity of experimentation necessary to generate the infinite number of variants/fragments recited in the claims and possibly screen same for activity and the lack of guidance/direction provided in the instant specification, this is merely an invitation to the skilled artisan to use the current invention as a starting point for further experimentation. Thus, undue experimentation would be required for a skilled artisan to make and/or use the claimed invention commensurate in scope with the claims.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al (US 2001/0018197), in view of Rabinowitz (US 5,096,594), as evidenced by Nevalainen et al (US 5,834,286)*

Wong et al teach an aqueous slurry is formed of a vegetable protein material having a pH of from about 3 to about 6. The protein material slurry is treated with an acid phosphatase enzyme, and optionally another phytase enzyme, at a temperature and for a time effective to degrade ribonucleic acids, and optionally phytic acid and phytates, in the protein material (see Abstract). In a preferred embodiment. a soy protein concentrate is prepared for use in the method of the present invention. Commercially available defatted soy flakes are washed with an aqueous solution having a pH of about 4-5, and most preferably at a pH of about 4.4 to about 4.6. The aqueous acidic solution leaches water soluble carbohydrate, minerals, phenolics, and other non-proteinaceous materials away from the soy protein, which is insoluble in the aqueous solution at its isoelectric point, leaving the soy protein concentrate [0017]. The solubilized protein material extract is then separated from insoluble vegetable matter such as cellulose and other vegetable fibers. It is inherent that inositol will be in water soluble fraction.

Wong et al do not explicitly teach the formation of inositol phosphate and inositol, pH less than 4, and separate inositol from the fraction.

Rabinowitz teaches a method of purifying cyclitols, particularly inositol by ion exchange column (see Abstract, claim 1). Rabinowitz also teaches that inositol was separated from other carbohydrates in plant juice extracts (col 2, lines 15-20).

As evidenced by Nevalainen et al, a mixture of phytase and a pH 2.5 acid phosphatase is capable of degrading inositolphosphate of phytates and phytic acid, inositolhexaphosphate IP6; inositolpentaphosphate IP5; inositil-tetraphosphate IP4; inositoltriphosphate IP3; inositol diphosphate IP2; inositol monophosphate IP1; to free inositol and inorganic phosphate (col 12, lines 12-20). For example, a phytase having phytate (IP6) as a preferred substrate may catalyze efficient hydrolysis of IP6 to IP5, IP4, IP3, IP2 but not to free inositol and inorganic phosphate. In turn, a pH 2.5 acid phosphatase may prefer simple phosphate substrate (e.g., IP5, IP4, IP3, IP2, and IP1) and may catalyze efficient hydrolysis of these substrates to free inositol and inorganic phosphates (col 12, lines 22-30). It is believed that by formulating the subject phosphatase of the invention within desired optimum ranges of phytase to pH 2.5 acid phosphatase activity the subject mixtures of the invention provide balanced enzyme mixtures having cooperative enzyme activity. The subject mixtures of the invention formulated in this manner may provide more rapid, efficient and complete release of greater amounts of free inositol and inorganic phosphate from phytate and phytic acid than produced in the same time under the same conditions of pH and temperature) by either of the constituent phosphatase enzymes (col 12, lines 28-40). It can be concluded that the probable hydrolytic end products of purified phytase enzymes are inositol di-and/or monophosphates. In contrast, purified acid phosphatase catalyzed degradation of phytate at pH2.5, producing inositol as an end product. These combined results suggested that in a commercial mixture of phosphatases, such as Finase, phytase alone is not sufficient to enable complete conversion of phytate to inositol and inorganic phosphate. Rather, the results suggested that inositol end products may be derived form the action of enzymes with substrate specificity similar to that of purified pH2.5 acid phosphatase.

The possibility was therefore considered that the products of phytate hydrolysis by phytase (i.e, IP5, IP4, IP3, IP2, IP1) might serve as useful substrate for acid phosphatase that would convert the inositophosphate into free inositol and inorganic phosphate (col 19, lines 37-56). The results show that purified phytase, while effective in mediating the hydrolysis of phytic acid, was less effective in catalyzing hydrolysis of other similar phosphate-containing substrates. In contrast, purified pH 2.5 acid phosphatase, while relatively effective in hydrolyzing simpler phosphate, was relatively ineffective in catalyzing hydrolysis of phytic acid. The results support the notion of a coorperative enzymatic mixture wherein the products of a purified phytase might serve as a substrate for a purified pH2.5 acid phosphatase so that free inositol and inorganic phosphate are the ultimate products of the reaction (col 20, lines 47-60). Nevalainen et al further teach that down-stream processing of the subject enzymes into a product may involve removal of cells and cellular debris (e.g., by centrifugation, filtration and the like), followed by concentration (e.g., by ultrafiltration, ion exchange or affinity chromatography and the like), or the starting material may be suitable for use in commercial processes after a simple purification (col 11, lines 18-25). Plant seeds are a rich source of minerals since they contain ions that are complexed with the phosphate groups of phytic acid (col 1, lines 23-27). The subject phosphatases are useful in commercial processes for releasing minerals from complexes with phytate in plant materials such as seeds and waste matter of milling, e.g., soybean meal (col 11, liens 54-58).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to separating the purifed inositol from the fraction using the technique as taught by Rabinowitz since Rabinowitz teaches that inositol were crystallized in high yield and high purity (col 2, lines 1-3). Regarding the limitation of pH less than 4, the result-effective

adjustment in conventional working parameters is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan, which is dependent on the crop and amount of insect control that is needed.

Claims 1, 3-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nevalainen et al (US 5,834,286), in view of Wong et al (US 2001/0018197), and further in view of Rabinowitz (US 5,096,594)

Nevalainen et al teach a mixture of phytase and a pH 2.5 acid phosphatase is capable of degrading inositolphosphate of phytates and phytic acid, inositolhexaphosphate IP6; inositolpentaphosphate IP5; inositil-tetraphosphate IP4; inositoltriphosphate IP3; inositol diphosphate IP2; inositol monophosphate IP1; to free inositol and inorganic phosphate (col 12, lines 12-20). For example, a phytase having phytate (IP6) as a preferred substrate may catalyze efficient hydrolysis of IP6 to IP5, IP4, IP3, IP2 but not to free inositol and inorganic phosphate. In turn, a pH 2.5 acid phosphatase may prefer simple phosphate substrate (e.g., IP5, IP4, IP3, IP2, and IP1) and may catalyze efficient hydrolysis of these substrates to free inositol and inorganic phosphates (col 12, lines 22-30). It is believed that by formulating the subject phosphatase of the invention within desired optimum ranges of phytase to pH 2.5 acid phosphatase activity the subject mixtures of the invention provide balanced enzyme mixtures having cooperative enzyme activity. The subject mixtures of the invention formulated in this manner may provide more rapid, efficient and complete release of greater amounts of free inositol and inorganic phosphate from phytate and phytic acid than produced in the same time under the same conditions of pH and temperature) by either of the constituent phosphatase

enzymes (col 12, lines 28-40). It can be concluded that the probable hydrolytic end products of purified phytase enzymes are inositol di-and/or monophosphates. In contrast, purified acid phosphatase catalyzed degradation of phytate at pH2.5, producing inositol as an end product. These combined results suggested that in a commercial mixture of phosphatases, such as Finase, phytase alone is not sufficient to enable complete conversion of phytate to inositol and inorganic phosphate. Rather, the results suggested that inositol end products may be derived form the action of enzymes with substrate specificity similar to that of purified pH2.5 acid phosphatase. The possibility was therefore considered that the products of phytate hydrolysis by phytase (i.e, IP5, IP4, IP3, IP2, IP1) might serve as useful substrate for acid phosphatase that would convertthe inositophosphate into free inositol and inorganic phosphate (col 19, lines 37-56). The results show that purified phytase, while effective in mediating the hydrolysis of phytic acid, was less effective in catalyzing hydrolysis of other similar phosphate-containing substrates. In contrast, purified pH 2.5 acid phosphatase, while relatively effective in hydrolyzing simpler phosphate, was relatively ineffective in catalyzing hydrolysis of phytic acid. The results support the notion of a coorperative enzymatic mixture wherein the products of a purified phytase might serve as a substrate for a purified pH2.5 acid phosphatase so that free inositol and inorganic phosphate are the ultimate products of the reaction (col 20, lines 47-60). Nevalainen et al further teach that down-stream processing of the subject enzymes into a product may involve removal of cells and cellular debris (e.g., by centrifugation, filtration and the like), followed by concentration (e.g., by ultrafiltration, ion exchange or affinity chromatography and the like), or the starting material may be suitable for use in commercial processes after a simple purification (col 11, lines 18-25). Plant seeds are a rich source of minerals since they contain ions that are

complexed with the phosphate groups of phytic acid (col 1, lines 23-27). The subject phosphatases are useful in commercial processes for releasing minerals from complexes with phytate in plant materials such as seeds and waste matter of milling, e.g., soybean meal (col 11, liens 54-58).

Nevalainen et al do not teach treating a slurry plant material, separating the soluble fraction from insoluble fraction, pH less than 4, or separating inositol from ionic fraction.

Wong et al teach an aqueous slurry is formed of a vegetable protein material having a pH of from about 3 to about 6. The protein material slurry is treated with an acid phosphatase enzyme, and optionally another phytase enzyme, at a temperature and for a time effective to degrade ribonucleic acids, and optionally phytic acid and phytates, in the protein material (see Abstract). In a preferred embodiment. a soy protein concentrate is prepared for use in the method of the present invention. Commercially available defatted soy flakes are washed with an aqueous solution having a pH of about 4-5, and most preferably at a pH of about 4.4 to about 4.6. The aqueous acidic solution leaches water soluble carbohydrate, minerals, phenolics, and other non-proteinaceous materials away from the soy protein, which is insoluble in the aqueous solution at its isoelectric point, leaving the soy protein concentrate [0017]. The solubilized protein material extract is then separated from insoluble vegetable matter such as cellulose and other vegetable fibers. It is inherent that inositol will be in water soluble fraction.

Rabinowitz teaches a method of purifying cyclitols, particularly inositol by ion exchange column (see Abstract, claim 1). Rabinowitz also teaches that inositol was separated from other carbohydrates in plant juice extracts (col 2, lines 15-20).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the technique of treating the slurry plant material, separating the soluble fraction from insoluble fraction of Wong et al in the invention of Nevalainen et al as Wong et al teach that Wong et al teach that the invention substantially reduce the phytic acid, phytate, and ribonucleic acid concentrations in the vegetable protein material. It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to separating the purifed inositol from the fraction using the technique as taught by Rabinowitz since Rabinowitz teaches that inositol were crystallized in high yield and high purity (col 2, lines 1-3). Regarding the limitation of pH less than 4, the result-effective adjustment in conventional working parameters is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan, which is dependent on the crop and amount of insect control that is needed.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

*This reference is cited merely to relay an intrinsic property and is not used in the basis for rejection *per se*.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Qiuwen Mi

/Patricia Leith/
Patricia Leith
Art Unit 1655
Primary Examiner